PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P11085 WO/MH	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/03040	International filing date *(day/month/year)* 11.07.2003	Priority date *(day/month/year)* 12.07.2002
International Patent Classification (IPC) or both national classification and IPC A23L1/29		
Applicant RECKITT BENCKISER HEALTHCARE (UK) LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 10 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.01.2004	22.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Tallgren, A Telephone No. +31 70 340-3933

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/03040

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

8-22	as originally filed
1-7	received on 21.07.2004 with letter of 21.07.2004

Claims, Numbers

1-15	received on 21.07.2004 with letter of 21.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☒ the description, pages: 23-25

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-15
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations

see separate sheet

1. The amended claims 1-15 fulfill the criteria set by article 34(2)b and is therefore accepted (old claim 7 and page 7 paragraph 1).

2. ITEM V

The following document is referred to:

CPA (closest prior art) EP-A-0583852

Both the application and CPA describe an ingestible composition containing polysaccharides, surfactant and colloidal silica.

The difference is, that in CPA there is no mentioning of ispaghula as the fiber. CPA produces a nutritious drink and current application produces a composition to alleviate constipation. Both CPA and current application are in a larger sense solving the same problem: dispersing composition to liquid. The difference is, that CPA has the problem of precipitation of gourd powder when put to water, but this is not really the problem addressed in CPA to choose correct ingredients. The main problem is to choose correct ingredients to achieve good taste. The problem of current application is to avoid to form a gel when put to water. A skilled person would not consider using ispaghula, because of the very well known gelling problem. Moreover, there is found a surprising effect to improve the wettability of ispaghula by using the special combination of colloidal silica with an ingestible surfactant. There is no document cited in the search report filed in time to suggest the use of above mentioned composition or to describe the surprising effect to ispaghula. Therefore a skilled person would not have a hint to use ispaghula in combination with colloidal silica and an ingestible surfactant to provide an easily dispersible composition.

Accordingly the amended claims 1-15 meet the requirements of Articles 33(2) and (3) PCT.

Improvements In and Relating to Medicinal Compositions

The present invention relates to medicinal compositions comprising fibre bulking agents.

Ingestible fibre- compositions for the relief of gastric and digestive dysfunctions are known. Examples of such compositions include granular psyllium husk fibre (ispaghula) intended to be stirred in measured amounts into a volume of liquid, usually water or soft drinks. After stirring, the drinking composition is intended to be quickly imbibed due to the propensity of the ispaghula to absorb water readily and swell to form a viscous gel-like mass. It is the property of water absorption which has the desired characteristic of fibre or saccharide-containing ingestible compositions for gastric and digestive dysfunctions. Once the fibre or saccharide-containing composition has absorbed water to produce the gel-like mass, the mass is relatively insoluble and fibrous, and is transported through the gut quickly with minimal digestion, helping to alleviate constipation and other digestive dysfunctions.

Other forms, such as capsules forms for ingestion, are also available, such capsules being designed to be broken down in the gut, wherein the released fibre or saccharide bulking agent absorbs water from the gut to form the viscous mass.

However, for beneficial ease-of-use properties, a particulate form is particularly advantageous to the end user, as this can be stirred into a volume of liquid, for a more pleasant taste, and the granular form of the fibre

absorbs water from the gut more quickly than a capsule form. However, there are a number of problems involved in using a granular form of the fibre-containing ingestible compositions.

Primarily, it is desirable for the ingestible compositions to disperse easily in liquid, for the user's convenience and/or so that the resultant drink is more palatable and/or easier to swallow. Any new composition must be as good as or, preferably, better than, existing compositions in this respect.

Secondly, the handling of some ingestible fibre-containing compositions is not straightforward. For example in commercial production ispaghula is milled then isopropyl alcohol and a granulating agent polyvinyl pyrollidone are added. These steps aid handling of the compositions during manufacturing, before the isopropyl alcohol is removed prior to packaging the product for sale. The granulation also aids the dispersion of the ispaghula into a volume of liquid, prior to ingestion. However, the use of the granulating agent and isopropyl alcohol increases the cost of production and the use of the isopropyl alcohol is undesirable from an environmental and a health and safety perspective.

Thus, from the foregoing, it is apparent that there is a need for the provision of an ingestible composition which comprises a fibre bulking agent, in which the ingestible composition disperses easily in an aqueous liquid and/or is of improved manufacture.

It has now been determined that an ingestible composition comprising a psyllium husk fibre bulking agent (ispaghula), colloidal silica in conjunction with an ingestible surfactant, can offer benefit in the manufacture of the ingestible composition, and can increase the rate at which the ingestible composition disperses in water or other ingestible liquid.

Therefore, according to the present invention there is provided an ingestible composition comprising ispaghula, colloidal silica and an ingestible surfactant wherein said composition is in a form so that in use it is dispersed in a liquid prior to ingestion.

The presence of both an ingestible silica and an ingestible surfactant can confer significant, eg synergistic, benefits. For example, the ternary composition of the ispaghula has outstanding wettability properties, and is easy to manufacture, for example by simple blending.

Suitably the fibre bulking agent is a natural ingestible fibre (by which term we include herein fibre extracts). Plant-derived fibre bulking agents from psyllium husk fibre (ispaghula) are used.

The ispaghula may comprise whole ispaghula seeds, but preferably at least part of the ispaghula comprises separated ispaghula seed husks. More preferably the ispaghula comprises at least 50% wt separated ispaghula husks, most preferably at least 95% wt separated ispaghula husks. Suitably the remainder of the ispaghula comprises other seed parts and/or other ispaghula plant materials. In preferred compositions the seed kernels themselves have been substantially removed to leave the husks.

Suitably the fibre bulking agent is present in the ingestible composition in an amount of at least 10wt%, preferably at least 30wt%, and most preferably at least 40wt% of the total weight of the ingestible composition.

Suitably the fibre bulking agent is present in the ingestible composition in an amount up to 90wt%, preferably up to 80wt%, and most preferably up to 75wt% of the total weight of the ingestible composition.

Suitably the colloidal silica is fumed or precipitated synthetic or natural silica. The silica may be amorphous or crystalline.

Suitably the mean particle size of the silica is at least 5nm, preferably at least 10nm.

Suitably the mean particle size of the silica is up to 5μm, preferably up to 0.75μm, more preferably up to 0.5μm, and most preferably up to 0.2μm.

One suitable silica material is Syloid 244 which is amorphous silica, has a mean particle size of about 3μm and is provided by W R Grace & Co. Another suitable silica materials is Silox 15,also from W R Grace & Co., and which has a mean particle size of about 4μm.

Another suitable silica material is Huber Zep 49 which is amorphous silica from J M Huber Corporation and contains about 1 wt% alumina.

Another suitable silica is Aerosil 200 from Degussa Company. It contains less than 0.05 wt% alumina and has a mean particle size of 12 nm.

The silica is colloidal silica (silicon dioxide), and a preferred silica is a colloidal silica which is sold under the trade mark CAB-O-SIL, by Cabot Inc, USA.

Suitably the specific surface area of the silica is at least $50m^2\ g^{-1}$, preferably at least $150m^2\ g^{-1}$.

Suitably the specific surface area of the silica is up to $400m^2\ g^{-1}$, preferably up to $300m^2\ g^{-1}$ most preferably up to $200m^2\ g^{-1}$.

Suitably the silica is present in the ingestible composition in an amount at least 0.01wt%, preferably at least 0.05wt%, more preferably at least 0.1wt% and most preferably at least 0.25wt%, of the total weight of the ingestible composition.

The upper limit of silica in the ingestible composition may be up to 11 wt%. Suitably the silica may be present in the ingestible composition in an amount up to 5wt%, preferably up to 2wt%, more preferably up to 1wt%, and most preferably up to 0.6wt%, of the total weight of the ingestible composition.

Preferably the ingestible surfactant is a polyethylene-, polypropylene-, or polyoxyethylene-based surfactant. Suitable polyethylene or polyoxyethylene-based surfactants include polyethylene glycols and polyoxyethylene sorbitan fatty acid esters (polysorbates).

Suitable polyethylene glycols have a molecular weight of between 200 and 40,000, preferably between 200 and 1,000, and more preferably between 200 and 600. Suitable

Claims

1. An ingestible composition comprising ispaghula, colloidal silica, and an ingestible surfactant wherein said composition is in a form so that in use it is dispersed in a liquid prior to ingestion.

2. An ingestible composition according to claim 1 wherein said composition in particulate or granular form.

3. An ingestible composition as claimed in any preceding claim wherein the particle size of the silica is between 5nm and 5μm.

4. An ingestible composition as claimed in any preceding claim wherein the specific surface area of the silica is between 50 and 400gm^{-2}.

5. An ingestible composition as claimed in any preceding claim wherein the silica is present in an amount of between 0.01wt% and 5wt% of the total weight of the ingestible composition.

6. An ingestible composition as claimed in any preceding claim, wherein the ingestible surfactant is a polyethylene-, polypropylene-, or polyoxyethylene-based surfactant.

7. An ingestible composition as claimed in claim 11 wherein the polyethylene-based surfactant is a polyethylene glycol.

8. An ingestible composition as claimed in claim 12 wherein the polyethylene glycol has a molecular weight of between 200 and 40,000, preferably between 200 and 1,000.

9. An ingestible composition as claimed in claim 11 wherein the polyoxyethylene-based surfactant is a polyoxyethylene sorbitan fatty acid ester.

10. An ingestible composition as claimed in claim 11, wherein the surfactant is a polyoxyethylene monostearate or a glycerol polyethylene glycol oxystearate.

11. An ingestible composition as claimed in any preceding claim wherein the ingestible surfactant is present in an amount of between 0.01wt% and 5wt% of the total weight of the ingestible composition.

12. An ingestible composition as claimed in claim 16 wherein the ingestible surfactant is polyethylene glycol and is present in an amount of between 0.1wt% and 2wt% of the total weight of the ingestible composition.

13. An ingestible composition as claimed in claim 16 wherein the surfactant is a polyoxyethylene sorbitan fatty acid ester and is present in an amount of between 1wt% and 2wt% of the total weight of the ingestible composition.19.

14. A method of making an ingestible composition comprising ispaghula, colloidal silica, and an ingestible surfactant, the method comprising the step of blending the ispaghula with the colloidal silica and the ingestible surfactant; preferably without the employment of isopropyl alcohol or more preferably of any solvent; and preferably

without the employment of polyvinyl pyrollidone or more preferably of any granulating agent.

15. An ingestible composition or its manufacture substantially as described herein.